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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,264	09/16/2003	Nicholas W. Warne	22058-544 (AM100664)	1450

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BOSTON, MA 02111

EXAMINER

HISSONG, BRUCE D

ART UNIT	PAPER NUMBER
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1646

MAIL DATE	DELIVERY MODE
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02/06/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/663,264

Applicant(s)

WARNE ET AL.

Examiner

Bruce D. Hissong, Ph.D.

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 5-12, 17, 19-26 and 28-56 is/are pending in the application.
- 4a) Of the above claim(s) 42-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 5-12, 17, 19-26, 28-41, 53-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

2. In the response received on 10/31/2007, the Applicants have added new claim 56. Therefore, claims 5-12, 17, 19-26, and 28-56 are currently pending. Claims 42-52 remain withdrawn as non-elected subject matter, and claims 5-12, 17, 19-26, 28-41, and 53-56 are the subject of this office action.

3. In the response received on 10/31/2007, the Applicants requested finality of the office action be withdrawn because claims 5 and 17 of the 1/11/2007 claim set had been amended in such a way as to change the scope of the invention, and therefore a final rejection was improper.

This argument has been fully considered and is not persuasive. It is noted that claims 5 and 17 were amended to include the limitation of human IL-11. However, the claims were examined with respect to this limitation because claim 5, part (a), required that the claimed composition comprise human IL-11. Thus, the amendments to the claims did not change the scope of the claims, and the final rejection was proper.

However, due to the new grounds of rejection set forth below, this office action is made non-final, rendering Applicant's request moot.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill

in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Rejection maintained

1. Claims 5-12, 17, 19-22, 25, 28-41, and 53-55 remain rejected under 35 USC § 103(a) as being obvious in view of the combination of Savastano *et al* ("Savastano") and Greenwood-van Meerveld *et al* ("Greenwood") as set forth on pages 7-10 of the office action mailed on 6/1/2006 and pages 3-4 of the office action mailed on 4/6/2007.

In the response received on 10/31/2007, the Applicants reiterate their previous argument that Greenwood is not available as prior art under 35 USC 102(a) because it represents the inventors' own work, as set forth in the declaration by Dr. Warne, in which he states that authors Greenwood-van Meerveld and Venkova were working under the supervision of either Dr. Warne or Dr. James Keith, who is a colleague of Dr. Warne. Dr. Warne also states that the Keith group was not involved in developing the claimed compositions or methods of use, but rather coordinated the testing of the formulations. The Applicants assert that the previous rejection incorrectly relied on *In re Katz*, because *Katz* holds that a statement by an inventor under oath is sufficient to establish the subject matter is his own original work, and his alone. For these reasons, the Applicants argue that the declaration by Dr. Warne is sufficient to provide an evidentiary basis for establishing that the claimed subject matter disclosed in the Greenwood publication is the inventors own work.

These arguments have been fully considered and are not persuasive. As set forth in MPEP 2132, a disclosure by "others" refers to any entity which is different from the inventive entity, and a prima facie case is made under 35 USC 102(a) if, within 1 year of filing, the invention is disclosed by "others". Furthermore, MPEP 2132 states that such a prima facie case under 35 USC 102(a) can be rebutted by a showing that the disclosure by "others" was derived from the Applicant's own work by way of an appropriate affidavit or declaration, as set forth in *In re Katz*. However, *Katz* describes a situation in which the declarant was both an inventor and an author of a reference applied as art, and specifically, a situation in which other authors of the publication filing a declaration to establish which portions of the work described in the reference originated with, or were obtained by the listed inventor of an application. The instant situation is not analogous because there is no inventor in common with the authorship of the Greenwood reference, and absent a statement from an author of the Greenwood reference describing the contributions of the authors, it cannot be said with certainty that the Greenwood reference is not prior art under 35 USC 102(a). For these reasons, the rejection is maintained for reasons of record. The Examiner suggests this rejection may be overcome by a properly filed declaration under 37 CFR 1.131.

2. Claims 23-24 and 26 remain rejected under 35 USC § 103(a) as being obvious in view of the combination of Savastano *et al*, Greenwood-van Meerveld *et al*, and Porter *et al*, as set forth on page 10 of the office action mailed on 6/1/2006, and page 4 of the office action mailed on 4/6/2007.

Applicants' arguments regarding the propriety of the Greenwood reference as prior art is discussed above. Because Greenwood has been determined to be prior art, as set forth above, the rejection is maintained for reasons of record.

New grounds of rejection

3. Claims 5-12, 17, 19-22, 25, 28-41, and 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savastano *et al* ("Savastano" - US 5,681,584), in view of Peterson *et al* ("Peterson" – Cytokine, 2000, 12:1769-1777).

The subject matter of the instant claims, and the disclosure of Savastano are discussed in the previous office action mailed on 6/1/2006. Briefly, Savastano teaches a composition for delayed-release oral dosage, but is silent regarding this composition comprising interleukin (IL)-11.

Peterson discloses oral administration of IL-11 in a murine model of contact hypersensitivity. Specifically, Peterson shows oral administration of recombinant human IL-11 in a liquid formulation (p. 1775, 2nd column), and shows that oral administration of recombinant human IL-11 reduces symptoms of contact hypersensitivity (p. 1772, 2nd column – p. 1773, 1st column; Fig. 7). Peterson is silent regarding a composition for delayed-release oral formulation.

However, it would have been obvious to a person of ordinary skill in the art, at the time the instant application was filed, to combine the teaching of Savastano and Peterson to practice the claimed invention of the instant application. By teaching a delayed-release drug delivery device for delivering proteins or polypeptides to the intestinal tract, Savastano would provide the motivation to coat a core containing proteins or polypeptides with the coating layers of the claimed invention. Peterson, by teaching that rhIL-11 can be orally administered and reduce the symptoms of contact hypersensitivity, would provide the motivation to incorporate rhIL-11 into the composition taught by Savastano.

The claims of the instant invention are drawn to the inclusion of several pharmaceutical excipients at various final percentages. As described above, Savastano teaches the use of a carbohydrate, amino acids such as methionine, methacrylic acid copolymers, HPMC, and talc. Savastano is silent in regards to the final percentage of each excipient in the final composition. However, optimization of excipients is common in the pharmacological arts. A person of ordinary skill in the art would have both

the motivation, and the technical expertise, to optimize the excipients listed above, and would have a reasonable expectation of success in doing so and arriving at the concentrations of the instant invention.

MPEP 2144.05 states:

“[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.” *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

The claims of the instant invention are also drawn to a pharmaceutical composition, as described above, in capsule form. Although Savastano teaches a composition in tablet form and is silent in regards to a composition in capsule form, pharmaceuticals in capsule form are well-known in the art. It would require routine optimization for a skilled artisan to adapt the composition of the instant invention to capsule form, and the skilled artisan would have both the motivation, and the technical expertise to do so with a reasonable expectation of success.

In summary, a person of ordinary skill in the art, at the time the invention was made, would have both the motivation and a reasonable expectation of success in creating the invention of the instant application by following the teachings of Savastano and Peterson. Savastano teaches a delayed delivery device for intestinal delivery of proteins and polypeptides that shares the features of the invention of the instant application. Peterson teaches that orally administered recombinant human IL-11 is effective for treating contact hypersensitivity, thus suggesting that orally administered IL-11 is biologically active. Thus, in view of these teachings, it would be obvious to one of ordinary skill in the art to incorporate recombinant human IL-11 of Peterson into the delayed-release device of Savastano.

4. Claims 23-24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Savastano *et al* (“Savastano” - US 5,681,584), in view of Peterson *et al* (“Peterson” – Cytokine, 2000, 12:1769-1777), and further in view of Porter *et al* (“Porter” - In Remington’s Pharmaceutical Sciences, 19th Ed. 1995, Chapter 93, p. 1653, 1st column, 9th paragraph – cited in the Office Action mailed on 12/7/2005). The subject matter of the instant claims and the disclosure of Savastano are discussed in a previous office action mailed on 6/1/2006. Briefly, claims 23-24 and 26 are drawn to the use of triethyl citrate as a plasticizer in the claimed composition. The disclosure of Peterson is described above. Savastano and Peterson do not teach the use of triethyl citrate as a plasticizer. However, Porter does teach that plasticizers are often incorporated into pharmaceutical compositions, and lists triethyl citrate as an accepted plasticizer.

Therefore, a person of ordinary skill in the art, at the time the invention was made, would have been motivated to combine the teachings of Savastano and Peterson with those of Porter to practice the invention of the instant application as claimed. The motivation to follow the teachings of Savastano and Peterson is described above. By teaching that triethyl citrate is a commonly used plasticizer, Porter would provide the motivation to incorporate triethyl citrate into the pharmaceutical composition of the instant invention. Thus, by following the teachings of Savastano, Peterson, and Porter, a person of ordinary skill in the art would have both the motivation to create the composition for delayed drug delivery as claimed in the instant invention, but also a reasonable expectation of success in doing so.

5. Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Savastano *et al* ("Savastano" - US 5,681,584), in view of Peterson *et al* ("Peterson" - Cytokine, 2000, 12:1769-1777), and further in view of McCoy *et al* - "McCoy", US 5,292,646 - cited in the IDS received on 12/12/2003)

Claim 56 is drawn to the claimed pharmaceutical composition for delayed-release oral administration, wherein said compound comprises des pro IL-11. The disclosures of Savastano and Peterson are discussed above; however neither references teaches des pro IL-11.

McCoy teaches an IL-11 polypeptide, wherein the N-terminal proline is deleted (see Example 1). The instant specification, on page 6, lines 6-9, defines des pro IL-11 as mature IL-11 in which the N-terminal proline has been deleted. Thus, McCoy discloses a des pro IL-11 polypeptide, and further discloses that this des pro IL-11 is biologically active (Example 2).

Thus, it would have been obvious to one of ordinary skill in the art, at the time the instant invention was filed, to incorporate the des pro IL-11 polypeptide of McCoy into the composition taught by Savastano. The motivation to do so comes from the teachings of Savastano and Peterson, which together provide the motivation to incorporate IL-11 into the composition of Savastano for use in oral administration. Furthermore, by teaching that des pro IL-11 is biologically active, McCoy would indicate to one of ordinary skill in the art that des pro IL-11 would be useful for treating disorders such as contact hypersensitivity. Therefore, by following the disclosures of Savastano, Peterson, and McCoy one of ordinary skill in the art would have both the motivation, and a reasonable expectation of success, to create a pharmaceutical composition for delayed-release oral formulation which meets the limitations of claim 56, and which comprises des pro IL-11.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Rejection of claims 5, 17, 19-20, 28-31, and 38-30 on the grounds of obviousness-type double patenting, as being unpatentable over claim 13 of co-pending Application No. 10/360,906, as set forth on page 5 of the office action mailed on 4/6/2007, is withdrawn in view of the abandonment of the '906 application.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hisson, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are

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unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647